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Predictive and retrospective modelling of airborne infection risk using monitored carbon dioxide

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Henry C. Burridge¹, Shiwei Fan², Roderic L. Jones², Catherine J. Noakes³, and P. F. Linden⁴

Abstract

The risk of long range, herein ‘airborne’, infection needs to be better understood and is especially urgent during the COVID-19 pandemic. We present a method to determine the relative risk of airborne transmission that can be readily deployed with either modelled or monitored CO₂ data and occupancy levels within an indoor space. For spaces regularly, or consistently, occupied by the same group of people, e.g. an open-plan office or a school classroom, we establish protocols to assess the absolute risk of airborne infection of this regular attendance at work or school. We present a methodology to easily calculate the expected number of secondary infections arising from a regular attendee becoming infectious and remaining pre/asymptomatic within these spaces. We demonstrate our model by calculating risks for both a modelled open-plan office and by using monitored data recorded within a small naturally ventilated office. In addition, by inferring ventilation rates from monitored CO₂ we show that estimates of airborne infection can be accurately reconstructed; thereby offering scope for more informed retrospective modelling should outbreaks occur in spaces where CO₂ is monitored. Well ventilated spaces appear unlikely to significantly contribute to airborne infection. However, even moderate changes to the conditions within the office, or new variants of the disease, typically results in more troubling predictions.

Keywords

Infection modelling, Airborne infection risk, Monitored CO₂, COVID-19, Coronavirus SAR-CoV-2

Introduction

The novel coronavirus disease (COVID-19), which causes respiratory symptoms, was declared a pandemic by the World Health Organization (WHO) on the 11th March 2020 — thereby marking its global impact. Transmission of such respiratory infections occurs via virus-laden particles (in this case the virus SARS-CoV-2) formed in the respiratory tract of an infected person and spread to other humans, primarily, via three routes: the droplet (or spray) route, the contact (or touch) route and the airborne (or aerosol) route (e.g. see^{1–3}). According to the WHO, “Airborne transmission is defined as the spread of an infectious agent caused by the dissemination of droplet nuclei (aerosols) that remain infectious when suspended in air over long distances and time”⁴. After some initial resistance, and significant pressure from the scientific community (e.g.^{5,6}), the WHO finally acknowledged the possibility of airborne infection for COVID-19 on the 8th July 2020⁷. In the latter part of 2020 multiple mutations to the SAR-CoV-2 virus conspired to give rise to a new variant, named B.1.1.7 (see, for example,⁸ for a more detailed discussion). This variant, now also known as the alpha variant, is currently thought to be significantly more infectious than pre-existing strains⁹ and is increasingly prevalent within the UK and other parts of Europe. At the start of 2021, with new more successful variants arising, COVID-19 infection levels remain worryingly high around much of the world. In our present article, we focus on assessing the risk of infection of respiratory diseases via the airborne route, taking COVID-19 as an example; ultimately, deriving a methodology for calculating the expected number

of secondary infections that might arise within any indoor space that is regularly attended by the same group of people, applicable to any airborne disease (with estimates for the duration over which infectors remain pre/asymptomatic.) We comment on the airborne infection risk for COVID-19 within open-plan offices under a variety of environmental conditions and include consideration of the alpha variant B.1.1.7.

The pioneering work of Wells¹⁰ and that which followed by Riley *et al.*¹¹ established methods, commonly referred to as the Wells-Riley model, for quantifying the risk of airborne infection of respiratory diseases. Unlike dose-response models, which assess the likely infection response to some (frequently cumulative) dose, Wells-Riley models typically report the complementary probability that no-one becomes infected. As such, these models do not rely on assessing

¹Department of Civil and Environmental Engineering, Imperial College London, Skempton Building, South Kensington Campus, London SW7 2AZ, UK.

²Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK.

³School of Civil Engineering, University of Leeds, Leeds, LS2 9JT, UK.

⁴Department of Applied Mathematics and Theoretical Physics, University of Cambridge, Centre for Mathematical Sciences, Wilberforce Road, Cambridge CB3 0WA, UK.

Corresponding author:

Henry C. Burridge, Department of Civil and Environmental Engineering, Imperial College London, Skempton Building, South Kensington Campus, London SW7 2AZ, UK.

Email: h.burridge@imperial.ac.uk

the cumulative exposure which could prove problematic when assessing the infection risk over durations of varied occupancy. Early formulations (e.g.¹¹) were restricted to indoor spaces which were in a steady-state with a known constant rate of ventilation of outdoor air. The requirement of steady-state is avoided by the formulation of the model presented by Gammaioni & Nucci¹². Rudnick & Milton¹³ further extended the practical application of the Wells-Riley model by negating the need to directly assess nor assume the rate of ventilation of outdoor air. Rudnick & Milton achieved this via the realisation that the risk of airborne infection could be directly inferred via measurements of CO₂ “if the airspace is well mixed”. We generalise the model of Rudnick & Milton relaxing the assumption of a well-mixed space and to further account for occupation profiles and activity levels which vary in time. The recent work of Peng & Jimenez¹⁴ highlights the ability to account for the expected differences between measurements of a gaseous scalar, e.g. CO₂, and virus particles; namely, particle deposition, viral decay and, potentially, active filtration. Herein, we do not account for these factors and in this regard, our results represent a conservatively high estimate of the risk.

For many airborne infections the likelihood of spread within the vast majority of indoor spaces, even over periods of a few hours, is reasonably low (as we show for the coronavirus SARS-CoV-2 and the resulting disease COVID-19). However, we suggest that there exists a significant proportion of indoor spaces which are, for the majority of each working day, attended by the same/similar group of people (e.g. open-plan offices and school classrooms), herein ‘regularly attend spaces’. Our model enables the likelihood of the spread of infection via the airborne route to be calculated (from either easily obtainable monitored data or modelled data) over multiple day-long durations. Hence, in the case of COVID-19 (for which infectors are estimated to remain pre-asymptomatic for 5-7 days) our model calculates the likely number of people that become infected during a period in which a pre/asymptomatic infector regularly attends the space.

We derive an extended airborne risk model, assess the risk of infection in a modelled open-plan office, and use monitored data from naturally ventilated office to estimate the infection risk. We describe retrospective modelling of an office, and then discuss the implications of our findings and draw our conclusions.

The Wells-Riley approach to airborne infection risk

The pioneering work of Riley *et al.*¹¹ defined the infectivity rate as

$$\lambda = \frac{I p q}{Q}, \quad (1)$$

where I is the number of infected people, p is the breathing (pulmonary ventilation) rate, Q is the ventilation (outdoor air supply) rate, and q is the unit of infection, quantum (see¹¹ for discussion), which varies significantly between disease, with activity level, and (as with all biologically derived parameters) with individual human beings. For many diseases and relevant activity levels, appropriate values of q have been determined and are reported in the literature (e.g.^{15–17}) – however, significant uncertainties are associated with these values. Moreover, the variability

due to individuality is challenging to reflect, as we return to discuss later. In particular, high values of risk are obtained from quanta generation rates derived from so called ‘superspreading events’ (e.g. see¹⁷) — we choose not to focus on such cases but note that should we have done so then the risks reported herein would be dramatically increased (see, for example, table 1). For a given demographic and activity level within the space the breathing rate p can be taken as constant and values are widely reported in the literature, the number of infected people I is an input to the model usually taken to be constant.

Riley *et al.*¹¹ were no doubt aware of the significant challenges in measuring, or even inferring, the outdoor air supply rate to a given indoor space (see Appendix). Instead, it was chosen to report the model in a form that can only be applied to indoor spaces for which the air is relatively well-mixed and the flows are in steady-state. Under these restrictive assumptions the classical Wells-Riley equation is recovered, namely that the likelihood, P , that infection spreads within a given indoor space during a time interval T is

$$P = 1 - \exp\left(-\frac{I p q T}{Q}\right). \quad (2)$$

A model for airborne infection risk in transient spaces with variable occupancy and activity levels

We present a simple model to estimate airborne infection risk which is capable of both exploiting data of the environmental conditions concerning the ventilation (i.e. CO₂ measurements), and accounting for occupancy levels that vary in time. As the insightful work of Rudnick & Milton¹³ highlighted, airborne infection can only occur through the breathing of rebreathed air that is infected. It is important to note that respiratory activity, e.g. breathing, results in a complex multi-phase flow being exhaled. Relative to inhaled air, exhaled air is typically warmer, of higher moisture content (both in the form of vapours and droplets), richer in CO₂, and contains more bioaerosols of which some may be viral particles. The fate of viral particles is of particular relevance to estimating infection risk, and determines via which of the three routes (droplet, contact or airborne) infection might occur, see^{2,3}. Those virus particles held in larger droplets may either be directly sprayed onto another individual (risking transmission via the droplet route) or fall to surfaces (potentially giving rise to transmission via the contact route). Following the WHO definition⁴, virus particles that might give rise to transmission via the airborne route must remain “suspended in air over long distances and time”. Therefore, the viral aerosols that can give rise to airborne infection (transmission via the airborne route) will be largely carried with the gaseous emissions exhaled. Directly detecting the presence of viral aerosols within air is challenging, costly and impractical to implement at scale. However, gaseous emissions exhaled by persons are relatively rich in CO₂, and CO₂ sensors of suitable accuracy (say ± 50 ppm) are easily obtained for a moderate cost. Hence monitoring CO₂ as a proxy for air that has the potential to be carrying viral aerosols, whilst being far from a perfect tracer, has

not only legitimate scientific grounds but is also practical to implement at scale.

Within most indoor spaces human breathing is the dominant source CO_2 and so the fraction f of rebreathed air can be inferred from the ratio of the CO_2 concentration within the space (above outdoor levels which we denote C_0) to the concentration of CO_2 added to exhaled breath during breathing, C_a , giving (see¹³)

$$f = \frac{C - C_0}{C_a}, \quad (3)$$

where C is the measured CO_2 within the space. Denoting the number of people n within the space and taking the occupancy to be constant gives the fraction of rebreathed air that is infected as $f I/n$. Note that estimating the likelihood of airborne infection via monitored CO_2 , from which the fraction of infected rebreathed air is estimated (e.g.¹³), makes no stronger assumptions than are already implicit within the classical formulation of the Wells-Riley equation (2). Within the Wells-Riley equation the ratio, $(Ip)/Q$, is the fraction of infected air estimated to be within the space while the formulation of Rudnick & Milton¹³ expresses it as $(fI)/n$. In both formulations the estimate of the fraction of infected air is translated into a likelihood of infection rate via the quanta generation rate. The quanta generation rates utilised in most studies (including the present study) are deduced from data concerning actual far-field infection events. Obviously, these infection events occur as a result of the full physics governing the complex transport of viral particles. As such, the empirical data (underlying the estimates of quanta generation rates) implicitly accounts for some of the differing physics expected to arise between the transport of hypothesised gaseous infectious air (required by Wells-Riley based models) and the actual transport of infectious particles — which for airborne infection to occur must (by the definition of the transmission route) be able to be ‘suspended in air over long distances and time’.

Rudnick & Milton¹³ chose to express their result as

$$P = 1 - \exp\left(-\frac{I}{n}q \int_0^T f dt\right) = 1 - \exp\left(-\frac{I}{n}q \bar{f} T\right). \quad (4)$$

As they point out, this result “has very general applicability; it is valid for both steady-state and non-steady-state conditions and when the outdoor air supply rate varies with time”. Furthermore, we highlight that their assumption of a well-mixed space is unnecessary. The fraction of rebreathed air, f , is based on a point measurement of CO_2 which, assuming human respiration is the dominant source of CO_2 (entirely reasonable in the absence of other sources, e.g. unvented combustion), provides, at any instant, a good estimate of the fraction of air at that point within the space that has already been breathed by another individual. This point measurement can be integrated according to equation (4) to give the likelihood that a person (at the same location as the CO_2 sensor within the space) becomes infected assuming only that the infected air is relatively well-mixed within the uninfected rebreathed air, i.e. it does not require that all the air within the space is well-mixed. This implies that, where multiple CO_2 sensors within a single indoor space (inevitably) give different readings, airborne infection

risk can be assessed without violation of the modelling assumption being implied; in fact, the different readings within the space could be exploited to obtain estimates of the spatial variation in risk.

We wish to extend the generality of equation (4) with greater application in mind, in particular to account for occupancy levels that vary in time. The likelihood that airborne infection occurs within a given space can be determined from

$$P = 1 - \exp\left(-\int_0^T \lambda dt\right) = 1 - \exp\left(-\int_0^T \sigma(n) f_i q dt\right), \quad (5)$$

with, in the general case, the fraction of infected air f_i within the space being determined by solution of

$$\frac{df_i}{dt} = \frac{Ip}{V} - \frac{f_i Q}{V}, \quad (6)$$

where V is the volume of the indoor space which is typically easily estimated, and $\sigma(n)$ is determined based on whether the space is occupied or unoccupied: $\sigma(n) = 1$ for $n > 0$ and $\sigma(0) = 0$. For a derivation of equation (5) from first principles see Appendix . With suitable selection of the time at which to initiate investigation, the initial condition $f_i(0) = 0$ will frequently be suitable; typically values for the breathing (pulmonary ventilation) rate p can be sourced from the literature, and from monitored CO_2 and occupancy levels the ventilation rate Q can be estimated from equation (18), although as discussed in Appendix such estimates are subject to considerable noise. In spite of this noise, when CO_2 is monitored and occupancy levels are available then solution of equation (5) is only lacking knowledge of the time series of the number of infectors I within the space. Note that solution of the full system of equations, e.g. equations (18), (5) and (6), does require the assumption that the air within the space be approximated as well-mixed because one is required to calculate the ventilation rates explicitly; unlike simpler models e.g. equations (4) and (7) which do not. Where retrospective modelling is being undertaken to assess a particular outbreak, or spreading event, estimates of these data may be available and attempts to apply the above might prove useful and we turn our attention to informing these cases in our result section. However, with a focus on predictive modelling which, by definition, requires some assumption regarding the presence of infectors $I(t)$, we now consider some appropriate assumptions.

We will either assume that occupants arrive and leave over realistic periods of time (i.e. we model them to not all arrive and leave at once), or our monitored data show this to be so, and thus there exists at least two reasonable principles by which to establish the presence of infectors, $I(t)$. At one extreme, assume that the infector is always the first to arrive and the last to leave. Alternatively, one could assume that there is always a constant proportion of the (current) occupants infected such that when the space is occupied to design capacity there is a single infector (this results in the number of infectors, I , taking non-integer values outside full design occupancy which is inconsequential). Should one choose to assume the former, there is potential that risks are over estimated reported for scenarios in which occupancy is decreased, or equivalently by allowing more occupants

one could under report the risk of the space since a lesser proportion of the occupants are infected — in the absence of knowledge as to who is infected, this cannot be reasonable for comparison of risk with different occupancy levels. As such, we choose to make the latter assumption, i.e. there is always a constant proportion, α , of the (current) occupants infected, i.e. $I(t) = \alpha n(t)$. Doing so renders $I(t)/n(t) = \alpha$ as constant or, alternatively, that the proportion α of rebreathed air that is infected remains constant, and as such we can write the likelihood of airborne infection in a far simpler form that still allows for variable occupancy, namely

$$P = 1 - \exp \left(- \int_0^T \sigma(n) f \frac{I}{n} q dt \right), \quad (7)$$

where we choose to include presentation with the fraction I/n within the integral to emphasise that both the numerator and the denominator vary in time. Making the assumptions that result in equation (7) being valid not only seems reasonable for predictive modelling but it enables the work of Rudnick & Milton¹³ to be extended to predict the airborne infection risk, based on either modelled or monitored CO₂ data, within indoor spaces that also have variable occupancy levels, crucially, without need to solve the more general equation (5). To solve equation (5) generally, one is required to solve equation (18) to estimate the volume flux as an input to then enable solution of equation (6); doing so requires monitored occupancy levels, CO₂ levels, and relies on the (temporal) gradients in monitored CO₂ levels. Presented in the form of equation (7) and noting $I(t)/n(t) = \alpha$, highlights that precise occupancy levels are not required for the assessment of infection risk, only knowledge of the occupied periods is required.

Throughout this study we choose to set α such that there is a single infector present, i.e. $I(t) = 1$, when the space is occupied to design capacity, N_d , which gives $\alpha = I(t)/n(t) = 1/N_d$. Doing so is as reasonable choice as any other but we note that should comparison of airborne infection risk between separate indoor spaces of differing design capacity be desired then alternate choices should be made. The applicability of the choices to enable predictive modelling via equation (7) will be highlighted throughout our results section, and we then further solve the equations in more general form.

Quantifying the relative risk for changes in environmental management

To examine the effects of a particular change in conditions within a given indoor space, e.g. change in ventilation rate, occupancy level/behaviour, etc., it is informative to define a ‘base case’ scenario for which the likelihood of infection during a time interval T is P_0 and quantify the airborne infection risk of chosen scenarios relative to the base case. We can then define the risk of some test scenario relative to the base case as $RR = P/P_0$, denoting this relative risk as RR_A when a pre/asymptomatic is investigated, i.e. $T = T_A$. It is worth noting that the relative risk can be written as a ratio of Taylor series expansions of the exponential terms. Doing so can aid approximation since, when the integral $\int_0^{T_s} \sigma f \frac{I}{n} q dt$, is small, the leading order terms in the expansion dominate and the relative risk

ceases to be dependent on the quanta generation rate — a notoriously difficult quantity to parameterise which also varies widely between diseases. Hence for airborne infection risk assessment the leading order expansion for the relative risk can be reported as valid for all diseases (note that the duration T for which the approximation remains valid does change with disease). Moreover, for any given disease results for the relative risk can be reported with a greater degree of certainty, irrespective of the duration.

Defining absolute risk and the expected number of secondary infections for a given indoor space

An indoor space can be considered as contributing to the spread of a disease if an infected person attends the space for a duration over which it is more likely than not that they infect others. In the case that someone is showing symptoms of the disease it is reasonable to assume that they cease attending the space or that they be required to do so. Individuals can remain infectious and asymptomatic/presymptomatic for time periods of multiple days (which we denote as T_A) and this renders equation (4) unsuitable for quantifying this likelihood for most indoor spaces. However, for regularly attended spaces e.g. open plan offices and school classrooms, the probability P_A that someone becomes infected via the airborne transmission route (assuming an infected person attends the space) can be robustly determined via our formulation equation (7). To do so, time series data for the rebreathed air fraction (monitored or modelled), the occupancy level and quanta generation rate are required over the duration T_A . For a given disease, assuming the activity levels (per capita) remain broadly the same within the space, the quanta generation rate can be assumed constant. For real-world assessment, f and n can be obtained from monitored CO₂ and occupancy data, respectively. Moreover, for model cases this can easily be calculated. We demonstrate examples of this for model building spaces, and using monitored data an existing open plan office taking COVID-19 as a case study.

As elegantly pointed out by Rudnick & Milton¹³ their formulation equation (4) can be used to determine what they term a ‘basic reproductive number’ for an airborne infectious disease within an indoor space. Herein, we describe this as the expected number of secondary infections via the airborne route, S_I , that arise within an indoor space when an infectious individual is attending the space and everyone else is susceptible. For regularly attended spaces, this is simply calculated from the probability of someone becoming infected over the pre/asymptomatic period multiplied by the number of susceptible people, giving

$$S_I = (N_a - 1) \left[1 - \exp \left(- \int_0^{T_A} \sigma(n) f \frac{I}{n} q dt \right) \right], \quad (8)$$

where N_a is the total number of people that regularly attend the space. We earlier pointed out that calculations of the likelihood of infection via either equation (4) or via equation (7) do not require the assumption that all the air within the indoor space is well-mixed. However, for the expected number of secondary infections to be a meaningful estimate then equation (8) requires that the likelihood of infection to be representative of the risk through the occupied indoor space. If all the air within the space is well-mixed then this

is simply satisfied; otherwise, multiple CO₂ measurements should be taken, within the breathing zone, to assess the degree of variation.

To summarise our modelling, we have developed practical statistics to assess airborne infection via relative risk based scenario testing (RR), the absolute probability of infection (P_A), and the expected number of secondary infections for an indoor space (S_I). All of these can be calculated by obtaining/modelling representative CO₂ data. Moreover, for measured/modelled CO₂ distributions within the space, on assuming the infected & uninfected rebreathed air are mixed, these statistics can be calculated and their variation within the space investigated.

Determining appropriate quanta generation rates

As with all Wells-Riley based infection modelling an input parameter for which great uncertainty abounds is the quanta generation rate, q — with the novelty of COVID-19 this uncertainty is compounded. Given the uncertainty, we include results of scenario tests at various feasible levels of q , which span nearly four orders of magnitude. All of our choices regarding quanta generation rates stem from the data presented in the study of Buonanno *et al.*¹⁸. As a base case, which we deem appropriate for the regularly attended spaces on which we focus (namely, open-plan offices and class rooms) we take a value of $q = 1$ quanta/hr — this is obtained by taking $c_x = c_i c_v \approx 7 \times 10^6$ RNA/ml, where $c_i = \{0.1, 0.01\}$ is the ratio between infectious quantum and the infectious dose expressed in viral RNA copies, and $c_v = \{7 \times 10^7, 7 \times 10^8\}$ RNA/ml is the viral load measured in sputum. These values obtained by consideration that for most of the time, in most open-plan offices and classrooms, most of the occupants are sitting breathing with perhaps a small number vocalising — the data for whispered counting falls between these two activities and is rather more close to breathing — as such, for our base case, we take data for whispered counting from Buonanno *et al.*¹⁸ and use their results to map our selected values of c_x to values of quanta generation rates q . Moreover, we consider a scenario in which the occupants within the open-plan office or classroom are (on average) all vocalising/talking (e.g. a call-centre or noisy classroom), taking again $c_x \approx 7 \times 10^6$ RNA/ml gives $q \approx 5$ quanta/hr. In addition, we consider a scenario in which the viral load in sputum is somewhat reduced, i.e. $c_v \approx \{2 \times 10^7, 2 \times 10^8\}$ RNA/ml, giving $q \approx 0.3$ quanta/hr.

Mutations of the SARS-CoV-2 virus have given rise to a new variant, named B.1.1.7, which has become widely detected in certain geographical regions (within the UK in particular) in the latter part of 2020 (see⁸ for details). This variant, which has already spread across international borders, is believed to be potentially around 70% more transmissible than the, herein, ‘pre-existing’ strains of the virus^{9,19}. It is, as yet, unclear by which mechanisms the transmission of the new variant is increased; however, it is an important development which demands analysis. We therefore include estimates for the airborne infection of variant B1.1.7 within our results. To do so, we assume the increase in transmission of B1.1.7 via the airborne route might be proportional to the total increase and, for the

various scenarios considered, take quanta generation rates for the variant, q_v , to be 70% higher than those corresponding to pre-existing strains of the virus, i.e. $q_v = 1.7q$.

Predictive modelling of airborne infection using COVID-19 as an example

Application to a model open-plan office

By way of example, we first consider a moderately sized open-plan office, of floor area 400 m² and (a generous) floor-to-ceiling height 3.5 m, which is designed to be occupied by 40 people²⁰. We assume that occupants arrive steadily between 08:00 and 09:00 each morning, each take a one hour lunch break during which they leave the office, and leave steadily between 17:00 and 18:00 each day. While within the office we assume that (on average) each occupant breathes at a rate of approximately $p = 8$ l/min with a CO₂ production rate of 0.3 l/min, giving $C_a = 0.038$ and we take the outdoor CO₂ level to be 400 ppm¹³. As a base case we assume ventilation provision inline with UK guidance for office spaces, i.e. $Q_{pp} = 10$ l/s/p²⁰, or a total ventilation rate of $Q = 400$ l/s.

Our model run for this open-plan office gives, for the base case, the absolute risk of infection during a period of pre/asymptomatic COVID-19 infection as $P_A = 1.1\%$. If one had have taken the classical Wells-Riley model (2), taking there to always be a single infector present and T to be the simple sum of occupied hours (i.e. $T = 40$ hrs), the level of risk reported would have been $P = 1.3\%$, around 20% higher. We note the key benefit of our model is the ability to use monitored CO₂ and occupancy data as we demonstrate.

The impact of varied quanta generation rates We first examine the impact of varied quanta generation levels; namely, $q = \{1, 0.3, 5\}$ on the likelihood of airborne infection. Figure 1 plots the absolute likelihood that someone becomes infected within the office via the airborne route over the period during which an infector is expected to remain pre/asymptomatic, i.e. 5 working days (since the period of pre/asymptomatic infectivity for COVID-19 is estimated as 5–7 days). The plot shows that in the base case the absolute risk, P_A , of airborne infection within this open-plan office is just around 1.1% (or assuming a lower viral load is appropriate the risk drops to around $P_A = 0.3\%$). However, if the open-plan were a call-centre then this risk that someone becomes infection through attending work increases to above 5%. These results correspond to estimates for the quanta generation rates based on the work of Buonanno *et al.*¹⁸ on data for ‘pre-existing’ strains of the SARS-CoV-2 virus. In the latter part of the year 2020 mutations have gave rise to a new variant of the virus B1.1.7 which is already prevalent in some geographical regions. Within figure 1 dashed lines show estimates for the likelihood of airborne infection for the B1.1.7 variant based on the current data which suggest this variant may be 70% more effectively spread. Since for the scenarios being tested the likelihoods remain relatively linear in response to changes in infectivity the risks are increased by a factor of around 1.7 in all three scenarios, i.e. the for the base case scenario with variant B1.1.7 the airborne infection is predicted to be nearly 2%.

One can, of course, examine the relative risk of airborne infection; as expected from consideration of Taylor series

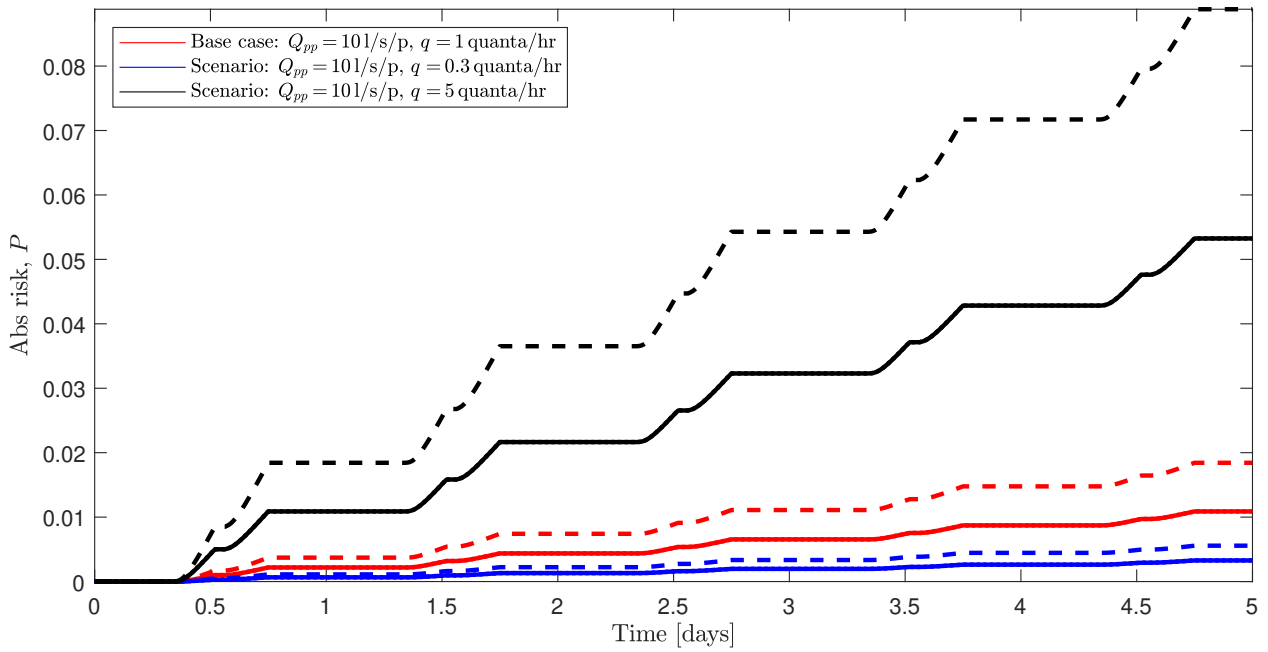


Figure 1. The variation in the likelihood of infection with time over the five day pre/asymptomatic period with ventilation inline with UK guidance, i.e. $Q_{pp} = 10 \text{ l/s/p}$. Solid curves mark the risk with differing quanta generation rates assumed for the pre-existing SARS-CoV-2 strains: blue denotes $q = 0.3 \text{ quanta/hr}$, red denotes $q = 1 \text{ quanta/hr}$, and black denotes $q = 5 \text{ quanta/hr}$. The correspondingly coloured dashed curves mark estimates for the variant B1.1.7 for which we take the quanta generation rates to be $q_v = 1.7q$.

expansions of the exponential terms, the results are broadly constant in time, with the relative risk taking an initial value of q/q_0 (or q_v/q_0), and then remaining dominated by the ratio of the quanta generation rate between the scenarios and/or variants. For example, in this office at the end of a pre/asymptomatic period, examining the scenario that the open-plan office changes to become equivalent to a call-center gives the relative risk as $RR_A = 4.9$ (for $q/q_0 = 5$, and taking $q_v = 1.7q$ gives $RR_A = 8.2$), and imagining that the appropriate viral load for the disease, for some reason, becomes lower gives $RR_A = 0.3$ (for $q/q_0 = 0.3$). One can see that for these cases the relative risk is well predicted by a linear approximation (taking only the first order terms in the Taylor series expansion of the probabilities), i.e. the relative risk is approximately equal to the ratio of quanta generation rates between the scenarios.

The importance of ventilation/outdoor air supply rates

The qualitative increase in the airborne infection risk within the office during a period of pre/asymptomatic infection for varied outdoor air supply rate per person, Q_{pp} , is broadly similar to that shown in figure 1. Over the full pre/asymptomatic period the base case (of course) again gives $P_A = 1.1\%$ for pre-existing strains of the SARS-CoV-2 virus. Doubling the ventilation rate per person to $Q_{pp} = 20 \text{ l/s/p}$ decreases the likelihood to $P_A = 0.6\%$, and decreasing the outdoor air supply rate per person to $Q_{pp} = 4 \text{ l/s/p}$ results in $P_A = 2.2\%$ (see table 1).

Examining the relative risk RR , for scenarios of changing ventilation rates, then RR takes an initial value of unity and only over time does the ventilation alter the accumulation of infected re-breathed air within the space. In this open-plan office, in the case that the ventilation is doubled from one scenario to the next, the relative risk reaches an

approximately steady value of $RR \approx 0.55$ around 6 hours after being occupied (see figure 2), and in the case of decreased ventilation ($Q_{pp}/Q_0 = 0.4$) then $RR \approx 2.0$ is reached after approximately 10 hours. At the start of each working day, as the office is reoccupied, the relative risk can be seen to deviate from, then return back to, its steady-state value (figure 2), this is as a consequence of transient effects — as the fraction rebreathed air increases at different rates in each scenario (due to the differing ventilation rates). Transient effects that occur at the end of the day do not affect the infection risk since the office is unoccupied. These deviations lessen each day as the transients have a smaller impact on the integral risk; the deviations are also more pronounced in the case that the ventilation is reduced, i.e. the black curve in figure 2.

The expected number of secondary infections for an open-plan office

We run our model for the expected number of secondary airborne infections (8) for a period of pre/asymptomatic infectivity (5–7 days, i.e. spanning 5 working days) varying both the quanta generation rate (of ‘pre-existing’ virus strains $q = \{0.3, 1.0, 5.0\} \text{ quanta/hr}$) and the outdoor air supply rate air supply rate ($Q_{pp} = \{4, 10, 20\} \text{ l/s/p}$). The results are presented in table 1 and suggest that, for these environmental conditions with quiet desk-based work being conducted, it is unlikely that an employee’s time within the office will significantly contribute to the spread of COVID-19 via the airborne route. However, if the RNA copies/viral load are as expected by Buonanno *et al.*¹⁸, i.e. $q \approx 1$ for quiet desk-based work, but the office is poorly ventilated then the expected number of secondary infections arising within this office may hover dangerously close to unity for pre-existing virus strains; should the B1.1.7 variant become prevalent then a single

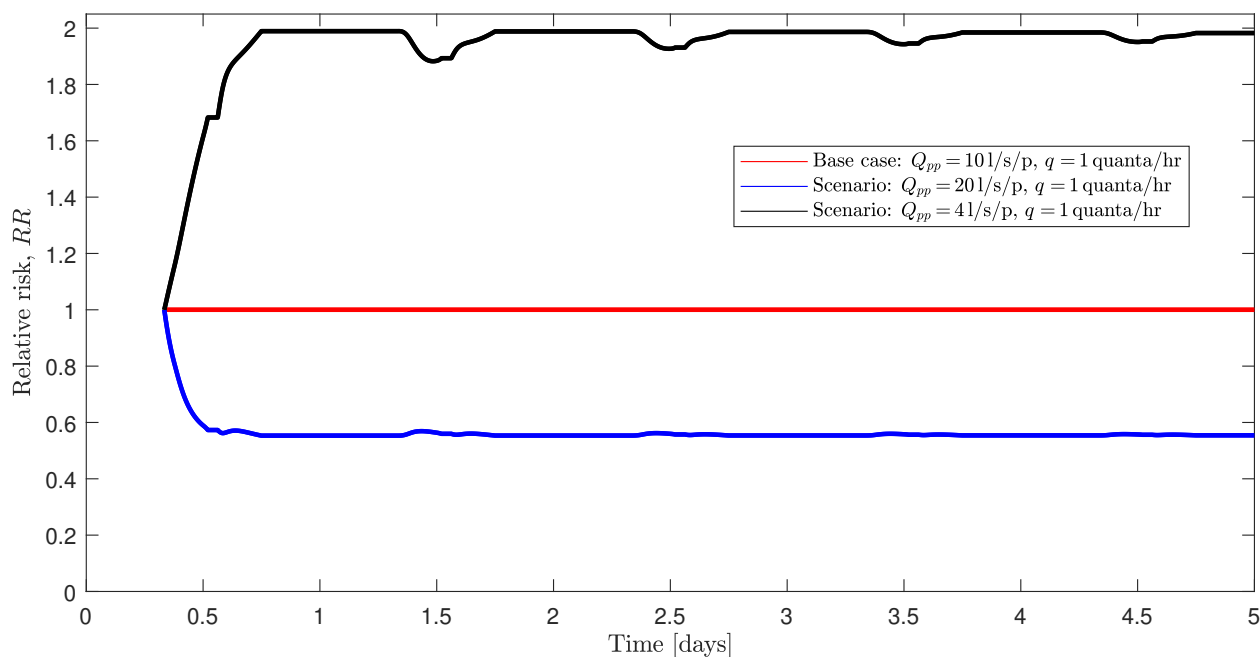


Figure 2. The variation in the relative risk, RR , of infection with time over the five day pre/asymptomatic period. The different curves highlight different scenarios, namely: the base case, $Q_{pp} = 10$ l/s/p (red), increased vent, $Q_{pp} = 20$ l/s/p (blue), and decreased vent, $Q_{pp} = 4$ l/s/p (black). The periodic deviations from the steady-state values of RR arise due to transient effects as the office is reoccupied each day.

Secondary infections, S_I	$Q_{pp} = 4$ l/s/p	$Q_{pp} = 10$ l/s/p	$Q_{pp} = 20$ l/s/p
$q = 0.3$ quanta/hr	0.25	0.13	0.07
Variant B1.1.7	[0.43]	[0.22]	[0.12]
$q = 1.0$ quanta/hr	0.84	0.42	0.24
Variant B1.1.7	[1.4]	[0.72]	[0.40]
$q = 5.0$ quanta/hr	4.0	2.1	1.2
Variant B1.1.7	[6.6]	[3.5]	[2.0]
$q = 20$ quanta/hr	14	7.6	4.4
Variant B1.1.7	[20]	[12]	[7.3]
$q = 100$ quanta/hr	35	26	18
Variant B1.1.7	[38]	[33]	[25]

Table 1. The expected number of secondary airborne infections, S_I , for COVID-19 arising within an open-plan office (floor plan of 400 m^2 and floor-to-ceiling height of 3.5 m) occupied by 40 people for 8 hrs each day over the period that a pre/asymptomatic person remains attending work. Bold text highlights the scenario (based on quiet desk-based work) taken herein as the base case; scenarios of $q = 5$ quanta/hr are intended to be representative of more vocal office environments, and higher quanta generation rate are intended to be indicative of superspreading scenarios. Values within square brackets provide estimates for the SARS-CoV-2 alpha variant B1.1.7 at quanta generation rates q_v relative to the pre-existing strains, i.e. $q_v = 1.7q$.

infection within the office could be expected to give rise to around 1.4 new infections just via the airborne route. Alternatively, if the office is used for particularly vocal activities, e.g. a call-center or sales office (i.e. making $q \approx 5$ more appropriate for pre-existing strains), then just through their occupation these spaces may significantly contribute to the spread of COVID-19 via the airborne route even when ventilated inline with current UK guidance — with the situation only worsened in the presence of the B1.1.7 variant.

To end this section, we note that Buonanno *et al.*¹⁸ report far higher quanta generation rates for ‘superspreaders’. The definition of a superspreader is unclear and far from unanimous. We note that the term may refer to specific combinations of the particular activity being undertaken, the environmental quality, and the biological response

of individuals. Within table 1, we include two sets of scenarios (based on $q = 20$ quanta/hr and $q = 100$ quanta/hr, respectively) which report the expected number of secondary infections that might arise within our office should some superspreading event occur within. The results are worrisome with the majority of employees becoming infected from the presence of a single infector in many of the scenarios examined. We hope that the conditions that might be required to give rise to superspreader events are unlikely to occur over durations comparable to a full pre/asymptomatic periods; if so, these scenarios may prove to be overly pessimistic.

The benefits of reduced occupancy The above results suggest, under certain conditions, occupation of an open-plan office may contribute to the spread of COVID-19 just

by the airborne route. This is troubling as the airborne route is perhaps the most difficult transmission route to mitigate against with appropriate ventilation being the primary mitigation strategy. Employers should help to mitigate the airborne spread of COVID-19 by ensuring ventilation systems are sufficient to comply with guidance and that they are properly maintained. However, large scale changes to the ventilation provision, for example to double the supply of outdoor air, are costly and will take time to implement appropriately (e.g. ensuring that the heating provision, and other factors, are also adequately adjusted or upgraded). One course of action that may be more immediately appealing is to consider keeping the occupancy reduced. For example, introducing week-in week-out working would result in the occupancy being halved. However, the ventilation system can be set to keep running at the full design capacity (which in our model office was $Q = 400 \text{ l/s}$ in the base case scenario). Doing so results in the expected number of secondary infections that might arise via the airborne route within our office being reduced by a factor of about four, because, all else being equal, in this example the probability of an infector being present is roughly halved compounded by the fact that there are half the number of people to infect. This fourfold reduction in secondary airborne infections is significant while the strategy provides opportunities for employees to attend the office in a manner which might be of practical benefit to themselves and their employer alike. Reducing the occupancy by a factor of r results in the expected number of secondary infections that might arise via the airborne route being reduced by a factor r^2 for all the scenarios considered herein.

Airborne infection risk from monitored data in open plan offices

To demonstrate the application of our model to indoor spaces with monitored CO_2 and occupancy data, the latter being obtained via analysis of video images of the office space. We were provided access to data recorded by the ‘Managing Air for Green Inner Cities (MAGIC)’ project (<http://www.magic-air.uk>). The data were recorded in a small office which had a design capacity of eight people, although during the times for which we were provided data never more than six people attended the office. The office is naturally ventilated with openable sash windows on opposite sides of the building. The floor area is approximately 37.6 m^2 and the floor-to-ceiling height is 2.7 m ; Song *et al.*²¹ provide full details of the monitored space and the monitoring equipment used but it should be noted the monitored office is not of a modern design and is not well-sealed nor well-insulated. For monitored data it is worth considering how to appropriately select the ambient CO_2 concentration, C_0 , since atmospheric levels do vary slightly and CO_2 sensors can exhibit a base-line drift over time. For all our analysis based on monitored CO_2 data we decided to allow the ambient CO_2 concentration to vary taking its value each day to be the mean value observed between 05:00 and 06:00.

The role of opening windows in reducing risk Figure 3 a) and b) show the occupancy profiles during two days in 2017. During 29th Sep the windows were opened on both sides of the building (providing an opened area of 0.24 m^2) at around

09:00 and remained so until after 20:00; whilst on 5th Oct the windows remained closed all day and we note that the spike in CO_2 at around 16:15 on this day corresponds to a brief visit during which 22 people were in the office. The monitored CO_2 profiles (figure 3 c) and d)) were obtained at six locations of differing heights (between 73 cm and 242 cm from the floor) and positions within the office. It is most striking that the CO_2 levels are markedly higher on 5th Oct when the windows remained closed. Crucially, these elevated CO_2 levels translate into increased risk of airborne infection for the occupants – in this case the risk of infection being approximately doubled on the day when the windows remained shut. In addition, at times (e.g. between about 14:00 and 17:00 on 25th Sep) there is a marked variation in measured CO_2 levels dependent on location. It follows that this variation in CO_2 is reflected in the infection risk levels which indicates that the location within the office at which one was breathing affected the risk of infection by around 20% on the day the windows were closed and a much more substantial variation on the day the windows were open.

Figure 4 a) shows the occupancy data for the monitored office over a five day period in September 2017. During this five day period the office windows were open for some significant portion of each day. The accompanying monitored CO_2 data is shown in figure 4 b) and it should be noted that data are missing between 13:30 and 19:00 on 27th September. The risk of airborne infection for COVID-19 is shown in the lower-pane with the risk rising gradually over the period of pre/asymptomatic infectivity reaching an absolute risk $0.059 \leq P_A \leq 0.064$ depending on where within the office the occupant would have been located. We note that two of the sensors were positioned very close to the windows. However, perhaps surprisingly, for the five day period the CO_2 concentrations measured in these positions were not significantly below that measured elsewhere within the office and the airborne infection risk estimated from the sensors near the windows was not systematically lower than those positioned in the centre of the room. One of the sensor placed close to the window, the data marked in orange in figures 3c), 3e), 4b), and 4c) does show levels which are significantly below the other sensors during 29th Sep — however, as figure 4c) shows over the five day period (25th–29th Sep) the impact is not drastic with the risk inferred from all sensors lying within $\pm 5\%$ of the mean. The expected number of secondary infections for the monitored office over this period is $0.3 \leq S_I \leq 0.32$ – reassuringly below unity and indicating that this naturally ventilated office was likely to have been receiving somewhere between 10 l/s/p and 20 l/s/p (see table 1). From examination of the monitored office during periods when the windows were closed the expected number of secondary infections might approximately double to $S_I \approx 0.6$. We note however, that these risks might be considerably higher for more modern well-sealed offices.

Retrospective modelling using COVID-19 as an example

In the following section we chose to examine a full pre/asymptomatic period within an open-plan office. However, the methodology for airborne risk evaluation we present is applicable to any shared indoor space for

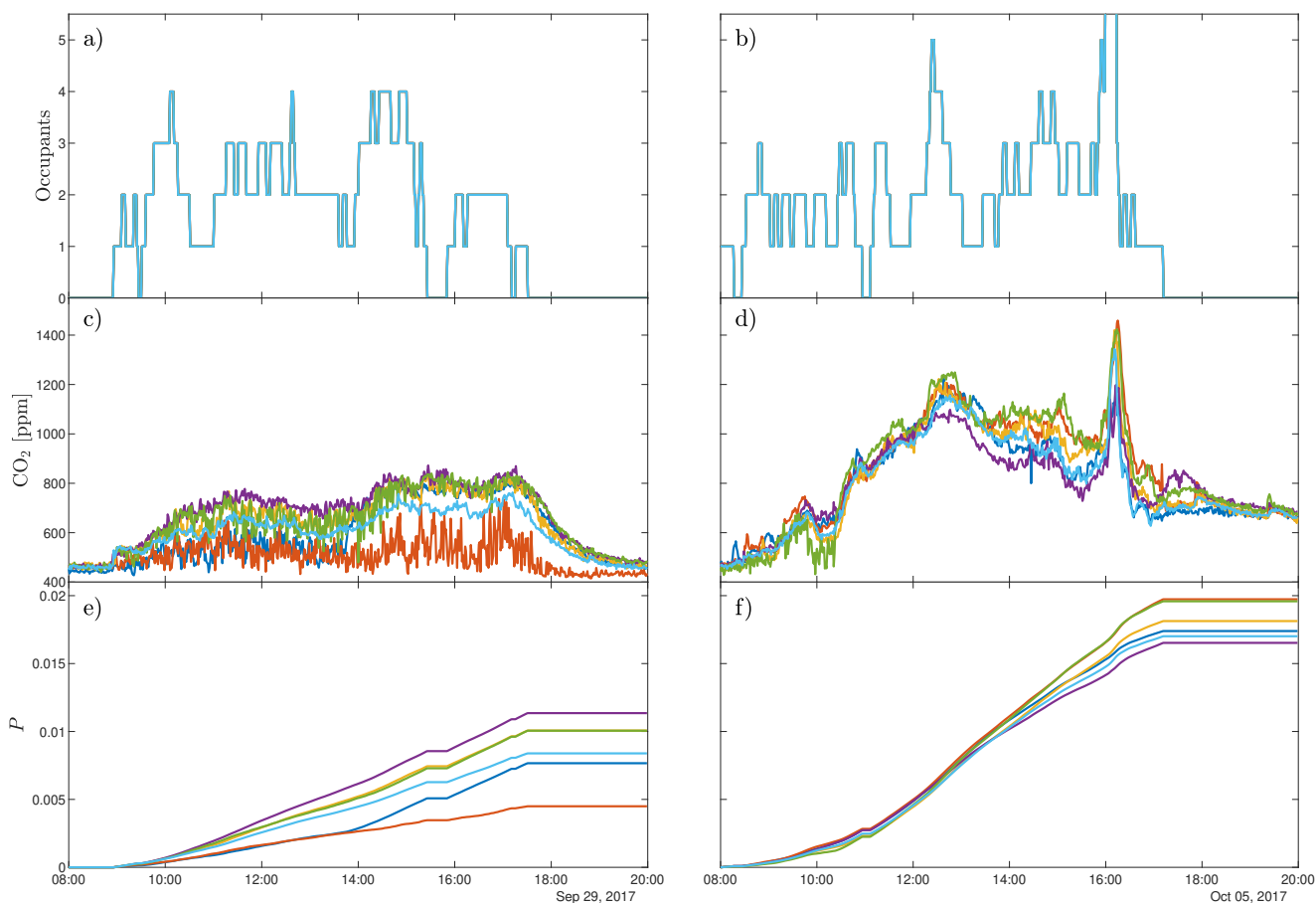


Figure 3. The intra-day variation in occupancy (upper panes, a) and b)), monitored CO_2 (middle panes, c) and d)) and the corresponding risk of airborne spread of COVID-19 (lower panes, e) and f)) during 29th Sep 2017 (left-hand panes, a), c) and e)) and 5th Oct 2017 (the right-hand panes, b), d) and f)). Data are plotted from six CO_2 monitors placed at various locations and heights (between 73 cm and 242 cm from the floor). On the 29th Sep (left-hand panes) windows on opposite sides of the room were opened (creating an opened area of around 0.24 m^2) from 08:00 until 20:00 whilst on the 5th Oct (right-hand panes) the windows remained closed all day.

which, whilst the number of occupants can vary throughout, the occupant population should only slightly exceed the observed maximum occupancy.

Where retrospective modelling of an outbreak is desired it is natural to assume that the infector's occupancy profile may be known (or at least estimated) and so invoking the simplifying assumptions that lead to our predictive model, equation (7), is likely to be inappropriate. In order to account for bespoke infector occupancy profiles one must return to the general equation for the likelihood of airborne infection, i.e. equation (5), which requires solution of both equation (18), to determine the ventilating flow through the space, and equation (6), to determine the amount of infectious airborne material present. This retrospective modelling requires that the ventilating flows are inferred from the monitored CO_2 and that these flows are then utilised to determine the dilution of the airborne infectious material being emitted by any infectors as and when they are present. As such, for this retrospective modelling it is necessary to assume that all of the air within the space is well-mixed. Where indoor concentrations are expected to vary spatially within a single space then multiple CO_2 monitors can be deployed to establish estimates of the errors introduced by the necessity to assume well-mixed air. The CO_2 data presented herein

is one such case, a naturally ventilated office with no mechanical means to generate a well-mixed environment. However, despite having sensors positioned both in the centre of the room and near the windows, over the full five day period (figure 4) the spatial variation in CO_2 concentration alone only changes the risk inferred from any sensor by at most $\pm 5\%$ of the mean; this despite the fact that for certain periods CO_2 concentrations varied considerably between the sensors.

To test the methodology of retrospectively inferring the risk from CO_2 measurements we select the data from only one of the sensors (plotted in green in figures 3 and 4); we do so to add the clarity of comparison between the results of different forms of analysis, the one sensor used was selected because it is relatively typical within the set of six sensors. We note that the results reported hereinafter have been tested for each of the six sensors with no notable differences arising. In order to establish the validity of the method, we first compare the results from the retrospective analysis to those of the 'true' predicted risk from our previous analysis. Within figure 5 the results of the risk from the predictive method are plotted as the black curve resulting in $P_A = 0.054$. However, when the same CO_2 data are used to solve equations (18) and (6), which are

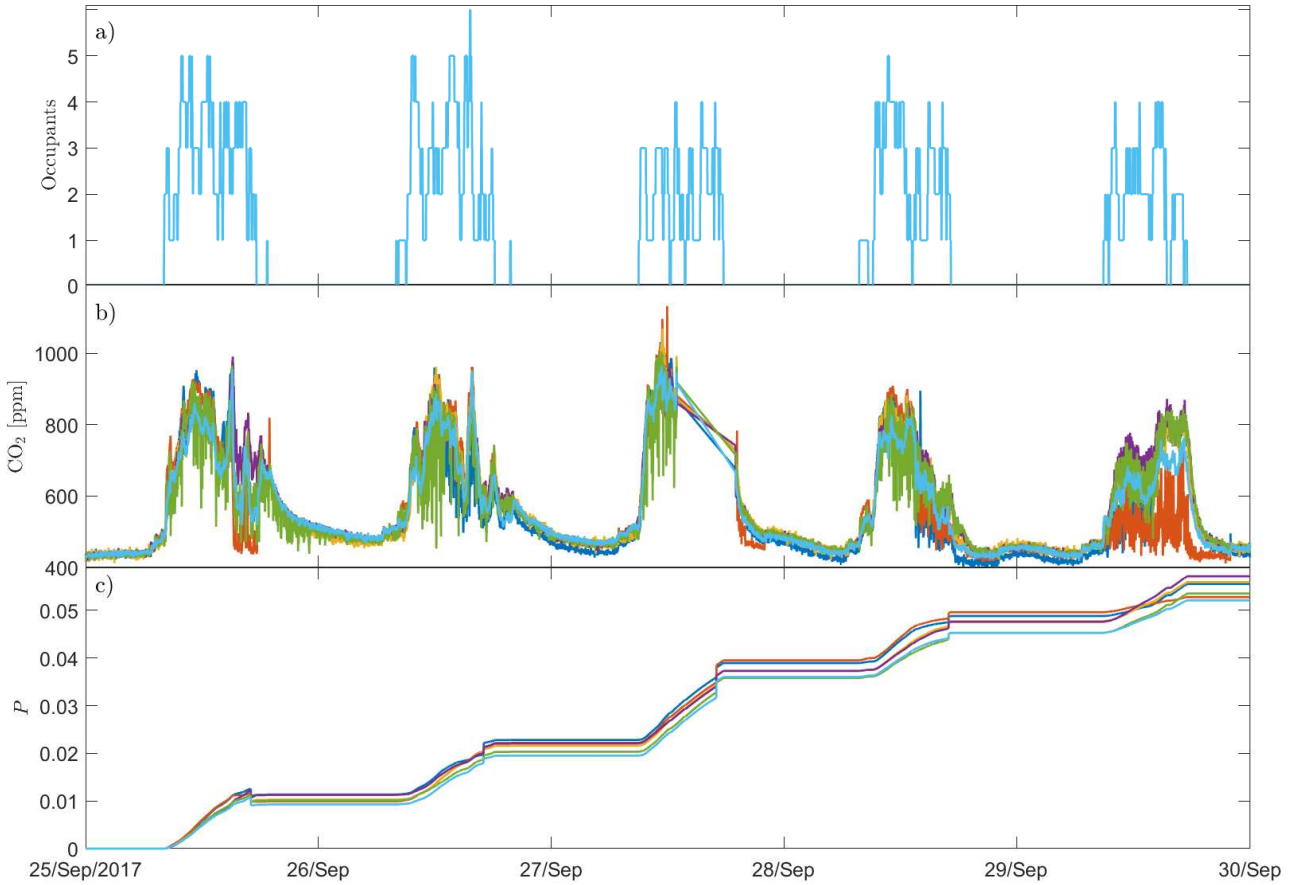


Figure 4. The variation in a) occupancy, b) monitored CO₂, and c) the corresponding risk of airborne spread of COVID-19, over a period of pre/asymptomatic occupancy of the monitored office. Data are plotted from six CO₂ monitors placed at various locations and heights (between 73 cm and 242 cm from the floor).

then substituted into equation (5) and integrated, i.e. the retrospective method (with the proportion of infectors, I/n , taken to be constant solely to enable direct comparison to the predictive method), the airborne infection risk (marked by the red curve) is significantly lower with $P_A = 0.044$. This difference arises because the retrospective method requires discrete observational data to be differentiated which introduces non-trivial errors, even when using a central differencing scheme. These errors can be avoided by fitting the observed data using cubic-spline curves, re-sampling the fitted spline curves at higher a frequency before differentiating and then time integrating to obtain the risk. However, to avoid observable errors in the risk one needed to re-sample our data, which were recorded every minute, at a frequency increased by a factor of at least 30, this proved computationally intensive even for a week long data set. As an alternate solution, passing these data through low-pass filters was found to effectively reduce these errors without significant loss of computation performance. For all our data, the airborne infection risk implied by the retrospective method was insensitive to the choice of low-pass filter (we tested the finite-duration impulse response, infinite-duration impulse response (IIR), and a third-order Savitzky-Golay filter in Matlab) and also relatively insensitive to the passband frequencies T_f^{-1} with $20 \text{ min} \leq T_f \leq 240 \text{ min}$ yielding notionally the same results (similarly in the case

of the Savitzky-Golay filter T_f denotes the duration of the filtering window).

Figure 5 also shows the retrospective airborne infection risk inferred from the CO₂ data, with a passband frequency and filtering window set by $T_f = 20 \text{ min}$, for an IIR (dotted cyan line) and a Savitzky-Golay filter (dotted magenta line), and with $T_f = 240 \text{ min}$ for an IIR (dashed cyan line) and a Savitzky-Golay filter (dashed magenta line) — all of which result in $P_A = 0.053$ (when rounded to two significant figures). As such, we can report that with appropriate filtering, airborne infection risk can be reconstructed retrospectively based on monitored CO₂ data. Based on all available data, the method appears to provide good accuracy when the CO₂ data is subjected to a low-pass filter, irrespective of the choice of filter, and exhibits an adequately low sensitivity to the choice of passband frequency, or filtering window.

For completeness, each night the CO₂ concentration within the office notionally reached ambient levels and these levels varied slightly from day-to-day, and we observed singularities in the implied flow rate when the denominator of the right hand term of equation (18), namely $(C - C_0)$, became zero. These could have either been avoided by setting the ambient CO₂ concentration artificially low but that would result in artificially high risk being reported. Instead, we replaced the denominator with $\max(C - C_0, 10^{-5})$ which both avoided the singularities and did

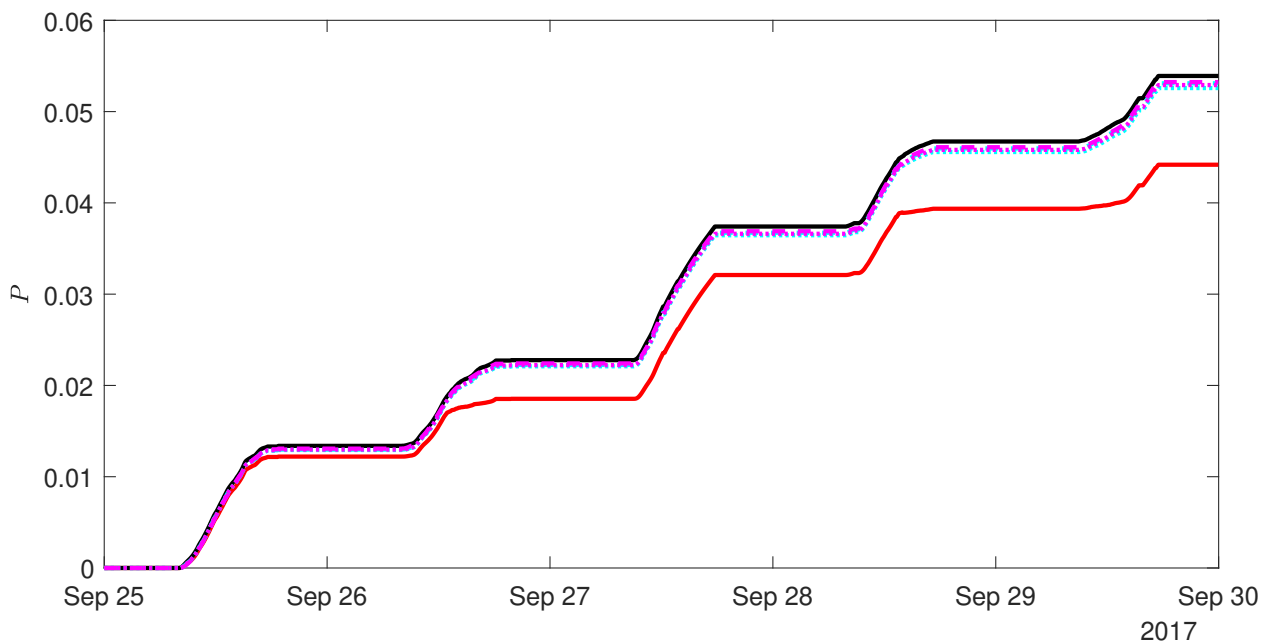


Figure 5. The variation in the likelihood of airborne infection risk, P , over a five day period based on CO_2 data from one sensor within the monitored office. The black curve shows the likelihood based on the predictive methodology equation (7), i.e. the same data from this sensor shown in figure 4. Estimates of the airborne infection risk, taking the same disease parameterisation and occupancy, but reconstructing the risk using the full equations using the raw CO_2 data are marked with by the red curve. Estimates of the airborne infection risk reconstructed using the full equations and CO_2 data subjected to a low-pass filter are marked with by cyan curves for infinite-duration impulse response filter and magenta curves for the Savitzky-Golay filter. Data are shown for passband frequencies, and filtering windows, based on $T_f = 20$ min (dotted curves) and $T_f = 240$ min (dashed curves).

not overstate the risk — this insertion can be justified upon realising that the tolerance of CO_2 monitors typically far exceeds 10^{-5} or 10 ppm. It is interesting to note that irrespective of the filtering we were never able to obtain estimates of the instantaneous ventilation flow rates, these typically fluctuated unreasonably in the range ± 100 ACH (air changes per hour). However, since these instantaneous ventilation flow rates only affect the likelihood via equation (6) which is then integrated twice, with respect to time, such unreasonable fluctuations do not, in practice, significantly affect estimates of airborne infection risk.

In order to demonstrate the flexibility of this method, we could examine the effects on the likelihood of airborne infection of a particular arrival and departure schedule of an infector during the five day period. However, it is widely accepted that the virulence of a COVID-19 infector might vary substantially during their pre/asymptomatic period and, as such, it is perhaps more relevant to consider such a case. The precise variation in a typical infector's virulence during the infectious period is not yet well evidenced so to demonstrate the ability to model such data, should it become available, we consider an extreme example where on only one of the pre/asymptomatic days the infector becomes significantly more virulent. We parameterise this temporal variation in infectivity via the quanta generation rate $q(t)$, and for reasonable comparison we ensure that the integral of $q(t)$ over the five days remains unchanged. Consider the arbitrary case that on day 3 the disease was particularly infectious with $q(t) = 3$ quanta/hr, while selecting $q(t) = 0.5$ quanta/hr for the other four days, thus ensuring that an average of $q = 1$ quanta/hr. In order to properly account for

varied quanta generation rates the subject of the integral in equation (5) needs to be evaluated via

$$\frac{df_i q}{dt} = \frac{I p q}{V} - \frac{f_i q Q}{V}. \quad (9)$$

The results are shown in figure 6. For reference the likelihood of airborne infection with constant $q = 1$ quanta/hr are shown for the predictive method, by the black curve, and the retrospective method (based on low-pass filtered CO_2 data), by the dashed magenta curve — both assuming I/n is constant, purely to enable comparison. Two blue curves mark the results for the case of variable infectivity being considered. For one, the more infectious day was taken to be the third day (27th Sep), and for the other it was taken to be the fourth day (28th Sep). Both blue curves initially indicate lower risk, for the days on which $q(t) = 0.5$ quanta/hr, and then show marked increases in the risk on the more infectious day before continuing to increase (at a rate less than that of the constant quanta generation rate). The risk for the case where the disease was more infectious on the 27th Sep finishes significantly above the risk of the constant quanta generation rate case; the opposite is true for the case where disease was assumed more infectious on the 28th Sep. This is simply because the integral CO_2 levels during 27th Sep were above the average for the five days and those on the 28th Sep were below the average. This is in line with expectations based on inspection of the system of equations since the risk is determined by the integral of $f_i q$ over time. Crucially, these results provide successful demonstration of the principles of retrospectively evaluating

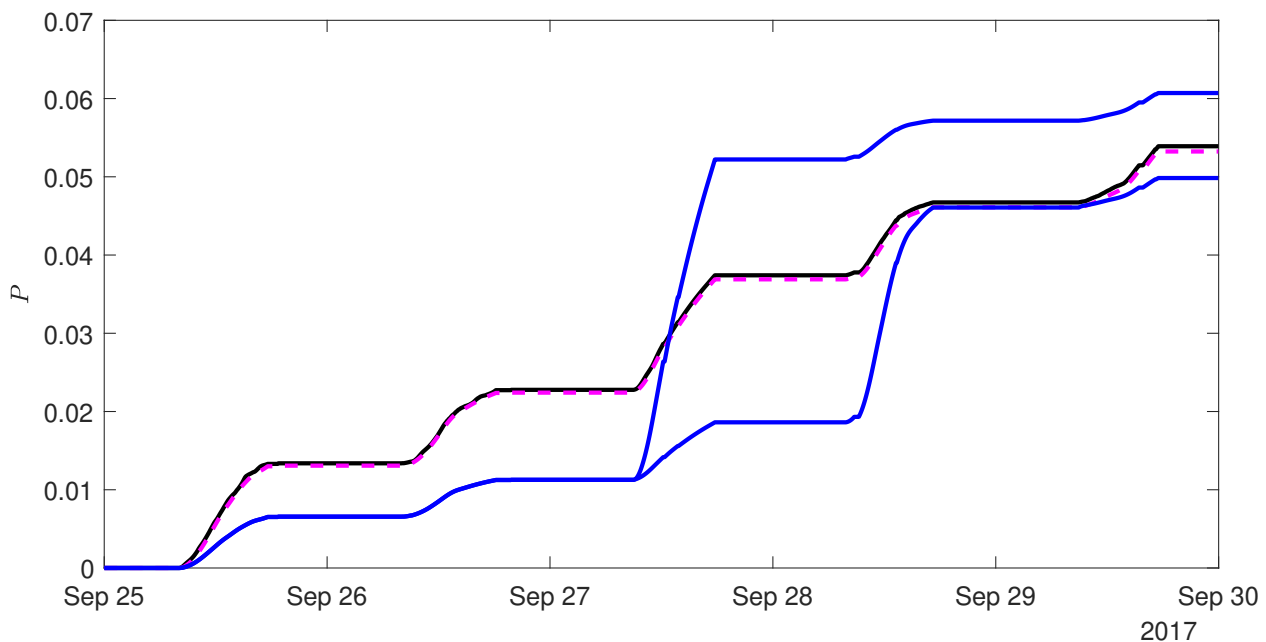


Figure 6. The variation in the likelihood of airborne infection risk, P , over a five day period based on CO_2 data from one sensor within the monitored office. For constant quanta generation rate of $q = 1$ quanta/hr: the black curve shows the likelihood based on the predictive methodology (7) and the dashed magenta curve the likelihood reconstructed from the low-pass filtered CO_2 data. The blue curves show the results assuming the disease is such that the infectivity on day 3 is greater than on the other four days but for fair comparison we parameterise the disease such that integral quanta over the five day period remains unchanged. In this case we chose values of $q = 0.5$ quanta/hr for the four days, rising to $q = 3$ quanta/hr on the more infectious day. The plot shows the final risk can be either above (when $q = 3$ quanta/hr on the second day, i.e. 27th Sep) or below (when $q = 3$ quanta/hr on the third day, i.e. 28th Sep) the results for the constant quanta case; with this being simply determined by whether rebreathed air was more prevalent (than the average over the full duration, here five days) during the more infectious period, or not.

the airborne infection risk for a general case based on actual CO_2 measurements.

Discussion and conclusions

Taking COVID-19 as an example relatively simple models have been derived to estimate the likelihood of airborne infection within indoor spaces which can account for variable occupancy levels, bespoke infector behaviours, and diseases for which the infectivity varies in time during the infectious period. Our models require only monitored or modelled data for CO_2 , occupancy & infector levels, and estimates of appropriate quanta generation rates (which in the most general case can vary in time). A modelled office and, separately, monitored data were used to demonstrate results.

We conclude that for open-plan offices, regularly attended by the same/similar people, which have ventilation provision in-line with UK guidance (e.g. ²⁰) then attendance of quiet desk-based work is unlikely to significantly contribute to the spread of COVID-19 via the airborne route. However, this changes should these spaces be poorly ventilated (e.g. 4 l/p/s) since then, through a single infected person attending the office, the expected number of people becoming infected via the airborne route is close to unity, and estimates rise well above for the SARS-CoV-2 variant B.1.1.7. (also now known as the alpha variant). Even for adequately ventilated spaces if the occupants are very vocal (e.g. a call-centre) then, in the presence of a single infector, one could expect attendance of the office to give rise to between two and four new COVID-19 infections, and so for these spaces we conclude

that attendance could significantly contribute to the spread of COVID-19 via the airborne route. Due to their ill-defined nature, we choose not to focus on superspreader scenarios but instead we primarily considered conditions more in-line with the median of the population. Should we have chosen to examine superspreaders then our results would have been more alarming.

Crucially, the above conclusions highlight that just by making readily achievable changes to the indoor environment can alter whether, or not, the attendance of work within an open-plan office might significantly contribute to the spread of COVID via the airborne route. These changes include, altering ventilation between rates that might actually be supplied to working offices, and changes in behaviours that can be expected to occur with different office usage. More successful variants of the virus, e.g. B.1.1.7, may only result in a greater number of the environmental scenarios giving rise to significant numbers of secondary infections. This highlights that as, and when, communal workplace practices are re-established there is a need to better mitigate against the airborne spread of COVID-19, while maintaining every effort to reduce the spread by other transmission routes.

Assessing and maintaining existing ventilation provision is the primary step in understanding the mitigation needs within an indoor space against for the airborne spread of COVID-19. To that end, we recommend that more widespread monitoring of CO_2 is carried out within occupied spaces. Doing so will provide a step towards practically assessing the actual ventilation provision being supplied

to these spaces. Where these spaces can be considered to broadly conform to our definition of a regularly attended space then we further recommend that occupancy profiles are recorded. In so doing, we provide a simple methodology with which to calculate the expected number of secondary COVID-19 infections arising, via the airborne route, within the monitored space. Irrespective of this, we believe that an indication of the rate of increase in infection risk (see equation (13)) should be considered for all indoor spaces; this can be expressed for the general case as $\lambda(1 - P) = f_i q(1 - P)$. In cases where estimates of the likelihood P are being recorded then the term, $(1 - P)$, can be included. Otherwise, a 'worst case' estimate can be easily obtained by taking the rate of increase in infection risk to be $f_i q$. However, there is no easily measurable proxy for $f_i q$ but where some predictive measure is required then an estimate can be obtained from consideration of our model, equation (7), giving $\lambda = (C - C_0) \alpha q / C_a$. For any given disease and chosen indoor space this shows that excess CO_2 determines the rate at which airborne infection risk is increasing, i.e. $\lambda \propto (C - C_0)$ with all other variables being independent of environmental conditions. Hence monitoring the excess CO_2 within spaces, for which occupants are enabled to make appropriate change, may be of significant benefit in mitigating airborne infection risk.

From a practical perspective it may be challenging to increase ventilation provision without significant time and investment, or without compromising occupants thermal comfort (which risks causing unwanted interventions). However, the formulation of our model makes it simple to demonstrate that reducing occupancy by a factor r and keeping the ventilation provision unchanged reduces the expected number of secondary infections by a factor r^2 for all of the scenarios considered. This observation may aid the safer re-establishment of open-plan offices where partial occupancy is of benefit and their environmental design is appropriate then introducing week-in week-out working may result in tolerable airborne infection risks for COVID-19 while offering benefits to both employees and employers.

Finally, we conclude that our model indicates that the risk of COVID-19 being spread by the airborne route is not insignificant and varies widely with activity level and environmental conditions which are predominantly determined by the bulk supply of outdoor air.

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Modelling from first principles

In order to demonstrate the underlying assumptions and highlight the limits of applicability we revisit the formulation

of the Wells-Riley equation^{10,11}. We wish to determine the likelihood, P , that infection spreads within a given indoor space during a time interval T . Denoting the probability that no one becomes infected during this time $P(0, T)$ gives that

$$P = 1 - P(0, T). \quad (10)$$

The number of infected people, I , is discrete (i.e. an integer) and since time is continuous we can consider a small period of time, δt , during which either no one becomes infected or one person becomes infected. Defining the infectivity rate λ (see below for a detailed discussion) gives the likelihood that one person becomes infected during this small time period as

$$P(1, \delta t) = \lambda \delta t. \quad (11)$$

Assuming that each infection occurs independently of the last

$$P(0, t + \delta t) = P(0, t)[1 - P(1, \delta t)] = P(0, t)[1 - \lambda \delta t]. \quad (12)$$

Rearranging and taking the limit $\delta t \rightarrow 0$ gives

$$\frac{P(0, t + \delta t) - P(0, t)}{\delta t} \equiv \frac{dP(0, t)}{dt} = -\lambda P(0, t), \quad (13)$$

integrating and substituting into equation (10) gives

$$P = 1 - \exp\left(-\int_0^T \lambda dt\right). \quad (14)$$

Hence the likelihood P can be evaluated for any known functional form of λ , crucially, as we go on to demonstrate, this can be inferred from data measured within indoor spaces which records occupancy level profiles and CO₂ concentrations.

The challenges of measuring ventilation rates or inferring ventilation rates from monitored CO₂

The original formulation of the Wells-Riley equation requires parameterisation of not only the quanta generation rate, q , but also evaluation of the infectivity rate which in the general case must be evaluated via the integral

$$\int_0^T \frac{I p q}{Q} dt. \quad (15)$$

Assuming broadly constant activity levels within a space the breathing rate, p , and (for a given disease) the quanta generation rate can be regarded as time independent. Furthermore it may be reasonable to assume the number of infected people within space remains unchanged if one is examining the likelihood of spread. Moreover, if the ventilation rate Q can be assumed constant and if the space is in steady-state then the probability of infection occurring during the period T can be simply expressed as

$$P = 1 - \exp\left(-\frac{I p q T}{Q}\right). \quad (16)$$

However, it is this last assumption that is most troubling since it is only reasonable if for a time exceeding the transient ventilation effects (which typically remain significant for

multiple hours): the opened area of all connections to the space (windows, doors, vents, etc...) remain unchanged, infiltration rates remain constant (or negligible), and the outdoor air supply rates are insensitive to changes that arise in the pressure differences between indoors and outdoors due to changes in temperature and wind — this makes application of equation (16) difficult. As we will discuss, measuring or inferring the ventilation rate within an operational occupied space is non trivial and hence evaluating equation (15) is impractical. The insightful work of Rudnick & Milton¹³ solved many of these challenges in assessing airborne infection risk and forms the basis for the modelling that we describe and develop.

The magnitude of infection risk changes with the seasons for numerous viral infections (including influenza) and these may arise for a variety of factors. These might include: changes in the viability of the virus if typical temperatures and/or humidity of indoor environments vary with the season, or if changing levels of natural UV light are significant and effect viability; changes in behaviour, for example, staying indoors more during colder seasons; changes due to the seasonal variations that occur in immunity²²; and, crucially for the airborne transmission route changes in ventilation (i.e. outdoor air supply) rates that occur as moderated indoor temperatures are demanded once outdoor temperatures vary with the season. We assert that this last factor, changing outdoor air supply rates, is highly significant yet it is poorly evidenced.

Outdoor air may enter an indoor space via a ventilation system, windows, doors, vents, cracks in the building fabric or, indeed, though the very fabric itself (i.e. many building materials, e.g. bricks, are porous). As such, there is significant scope for both intentional and unintended supply of outdoor air. Directly measuring the air flow through all of the potential pathways for any given indoor space is impractical. Pressure testing can be used to measure infiltration rates but cannot assess the ventilation rates in operational settings.

Indoors, human activity is typically the major source of CO₂ while outdoor CO₂ levels remain broadly constant. Therefore, if the rate of CO₂ production from human activity within a space can be estimated, CO₂ provides a suitable proxy from which to attempt inference of the ventilation/outdoor air supply rate within the space. Consider an indoor space in which both occupancy levels and CO₂ are monitored. If the activity levels of individuals remains broadly similar and the CO₂ monitored, C , can be regarded as indicative of the CO₂ levels throughout the space, i.e. the CO₂ is relatively well-mixed within the indoor air (note that only point measurements of CO₂ are practically possible), then since CO₂ is inert its conservation requires that

$$V \frac{dC}{dt} = n p C_a - Q (C - C_0), \quad (17)$$

where n is the number of people in the space and C_a is the volume fraction of CO₂ added to exhaled breath during breathing. As discussed, it is unwise to regard the ventilation rate as constant for most indoor spaces, i.e. $Q = Q(t)$, and this renders equation (17) non trivial to integrate analytically.

Thus if one wishes to examine the ventilation rate

$$Q = n p \frac{C_a}{(C - C_0)} - \frac{V}{(C - C_0)} \frac{dC}{dt}, \quad (18)$$

can be evaluated with monitored occupancy and CO₂ data, assuming a reasonable estimate of individuals CO₂ flux, $p C_a$, can be made (which in practice varies, in particular, with age, gender, and activity levels). However, as with all real-world data, the CO₂ signal is likely to contain some non-negligible level of noise and the dependence on dC/dt will, in some cases, render evaluation of ventilation/outdoor air supply rate via equation (18) unsuitable without considered filtering of the measured data.

An alternate approach is to examine the monitored occupancy data to determine the time at which the room becomes unoccupied. Assuming that the ventilation rate remains unchanged thereafter (which will only be the case if ventilation systems are left operational, and any changes in the ventilation/outdoor air supply rate due to the effects of wind and temperature variations are negligible) the CO₂ concentration within the space, assuming the air within remains relatively well-mixed, will decay exponentially. By exponential fitting to the monitored data during this period a ventilation/outdoor air supply rate can be inferred. However, curve fitting to real-world data is prone to variability due to choices of the input parameters (e.g. the period over which exponential decay to determine to be observed) and subject to influence from noise within the data, thereby rendering the results unreliable. Moreover, this process is hard to automate and so typically requires significant manual intervention, making it potentially unsuitable for the analysis of large data sets.

In summary, direct measurements of ventilation/outdoor air supply rates are extremely challenging. For this reason, and those described herein, we counsel that to assess airborne infection risks no attempts be made to directly assess outdoor air supply/ventilation rates to indoor spaces. Instead, we suggest widespread monitoring of CO₂ within spaces combined with measured/estimated occupancy profiles, which with application of our extensions to the work of Rudnick & Milton¹³ can be used to directly assess the airborne infection risk within a given space. Where required, simple modelling can be carried out to inform and assess practical mitigation strategies.

Author Contributions

We all work hard and produced this article together.

Competing interests

The authors declare no competing interests.

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